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Sheet 1 of 3

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Application Number 09/808,832

Filing Date March 15, 2000

First Named Inventor Copeland et al.

Group Art Unit 1653

Examiner Name J. Russell Russe

Attorney Docket Number PH-7134

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of

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U.S. PATENT DOCUMENTS

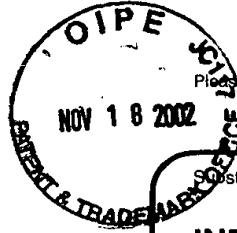
| Examiner Initials * | Cite No. ¹ | U.S. Patent Document | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Cited Column, Line, Where Relevant Passages or Exhibits FIGURES APPENDIX |
|---------------------|-----------------------|----------------------|--------------------------------------|---|---|--|
| | | Number | Kind Code ² (if known) | | | |
| JKR | AA | 5,962,216 | | Trouet et al | 10/5/1999 | 435/4 |
| JKR | AB | 4,703,107 | | Monsigny et al | 10/27/1987 | 530/330 |
| JKR | AC | 6,342,480 | | Trouet et al | 1/29/2002 | 514/18 |
| | | | | | | |
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FOREIGN PATENT DOCUMENTS

| Examiner Initials* | Cite No. ¹ | Foreign Patent Document | | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
|--------------------|-----------------------|-------------------------|---------------------|-----------------------------------|---|--|---|
| | | Office ³ | Number ⁴ | Kind Code ⁵ (if known) | | | |
| | | WO | 9600503 | | Merck & Co. Inc. | 1/11/1996 | |
| | | WO | 9605863 | | La Region Wallonne | 2/29/1996 | See AA & AC |
| | | WO | 9712624 | | Merck & Co. Inc. | 4/10/1997 | |
| | | WO | 9714416 | | Merck & Co. Inc. | 4/24/1997 | |
| | | WO | 9748725 | | Peptech Limited | 12/24/1997 | |
| | | WO | 9810651 | | Merck & Co. Inc. | 3/19/1998 | |
| | | WO | 9810795 | | Burnham Inst. | 3/19/1998 | |
| | | WO | 9816240 | | Liposome Co. Inc. | 4/23/1998 | |
| | | WO | 9818493 | | Merck & Co. Inc. | 5/7/1998 | |
| | | WO | 9846250 | | The Regents of the Univ. of CA | 10/22/1998 | |
| | | WO | 9902175 | | Merck & Co. Inc. | 1/21/1999 | |
| | | WO | 0033888 | | Coulter Pharmaceutical, Inc. | 6/15/2000 | |
| | | WO | 0059930 | | Merck & Co. Inc. | 10/12/2000 | |
| | | WO | 0064486 | ✓ | Veritas Medical Techn., Inc. | 11/2/2000 | |
| | | WO | 0071571 | | Boehringer Ingelheim | 11/30/2000 | |
| | | EP | 126685 | | Centre National de la Recherche Scientifique | 11/28/1984 | See AB |
| | | EP | 359347 | ✓ | Neox Corporation | 3/21/1990 | |
| | | UK | 2131813 | ✓ | Monsanto Co. | 6/27/1984 | |

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| Application Number | 09/808,832 |
| Filing Date | March 15, 2001 |
| First Named Inventor | Copeland et al |
| Group Art Unit | 16534 |
| Examiner Name | J. Russell-Russe |

Attorney Docket Number

PH-7134

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OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

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|---------------------|----------|--|---|
| JRL | 1 | TIMAR et al, "The antiproliferative action of a melphalan hexapeptide with collagenase-cleavable site" Cancer Chemotherapy Pharmacology, vol. 41, no. 4, 1998, 292-298 | 2 |
| JRL | | MASQUELIER et al, "Amino Acid and Dipeptide Derivatives of Daunorubicin. 1. Synthesis, Physicochemical Properties, and Lysosomal Digestion", Journal of Medicinal Chemistry, American Chemical Society, vol. 23, no. 11, 1980, 1166-1170. | |
| JRL | | DENMEADE et al, "Enzymatic Activation of a Doxorubicin-Peptide Prodrug by Prostate-Specific Antigen", Cancer Research, American Assoc. for Cancer Research, vol. 58, June 15, 1998, 2537-2540 | |
| JRL | | SAFAVY et al, "Paclitaxel Derivatives for Targeted Therapy of Cancer: Toward the Development of Smart Taxanes" Journal of Medicinal Chemistry, Am. Chem. Soc., vol. 42, 1999, 4919-4924 | |
| JRL | | MCGEEHAN et al, "Characterization of the Peptide Substrate Specificities of Interstitial Collagenase and 92-KDa Gelatinase Implications of Substrate Optimization" Journal of Biological Chem., vol. 269, no 52, Dec. 30, 1994, 32814-32820 | |
| JRL | | AIMES et al, Matrix Metalloproteinase-2 Is an Interstitial Collagenase, Journal of Biological Chemistry, vol. 270, No. 11, March 17, 5872-5876, 1995 | |
| JRL | | KURSCHAT et al, Tissue Inhibitor of Matrix Metalloproteinase-2 Regulates Matrix Metalloproteinase-2 Activation by Modulation of Membrane-type 1 Matrix Metalloproteinase Activity in High and Low Invasive Melanoma Cell Lines, Journal of Biological Chemistry, vol. 274, No. 30, 21056-21062, 1999 | |
| JRL | | GARBISA et al, Correlation of Serum Metalloproteinase Levels with Lung Cancer Metastasis and Response to Therapy, Cancer Research, 52, 4548-4549, 1992 | |
| JRL | | BOVEN et al, Doxorubicin Compared with Related Compounds in a Nude Mouse Model for Human Ovarian Cancer, Eur. J. Cancer, Vol. 26, no. 9, 983-986, 1990 | |
| JRL | | KNAUPER et al, Biochemical Characterization of Human Collagenase-3, Biological Chemistry, Vol. 271, No. 3, 1544-1550, 1996 | |
| JRL | | BROOKS et al, Localization of Matrix Metalloproteinase MMP-2 to the Surface of Invasive Cells by Interaction with Integrin $\alpha v\beta 3$, Cell, Vol. 85, 683-693, 1996 | |
| JRL | | MOSES et al, Increased Incidence of Matrix Metalloproteinases in Urine of Cancer Patients, Cancer Research, 58, 1395-1399, 1998 | |
| JRL | | CANAL et al, Human pharmacokinetics of N-L-leucyl-doxorubicin, a new anthracycline derivative, and its correlation with clinical toxicities, Clin. Pharmacol. Ther., volume 51, number 3, 249-259, 1992 | |
| JRL | | BOVEN et al, The anti-tumour effects of the prodrugs N-L-leucyl-doxorubicin and vinblastine-isoleucinate in human ovarian cancer xenografts, Br. J. Cancer, 66, 1044-1047, 1992 | |

Examiner Signature

Jeffrey E. Russell

Date Considered

December 3, 2002

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| OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS | | | | | |
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| <i>JRL</i> | | MCDONNELL et al, Role of matrix metalloproteinases in invasion and metastasis: biology, diagnosis and inhibitors, Cytotechnology, 12, 367-384, 1993 | | | |
| <i>JRL</i> | | BRUMMER et al, Matrix-metalloproteinases 1, 2 and 3 and their tissue inhibitors 1 and 2 in benign and malignant breast lesions: an in situ hybridization study, Virchows Arch, 435, 566-573, 1999 | | | |
| <i>JRL</i> | | MACDOUGALL et al, Contributions of tumor and stromal matrix metalloproteinases to tumor progression, invasion and metastasis, Cancer and Metastasis Reviews, 14, 351-362, 1995 | | | |
| <i>JRL</i> | | DE JONG et al, Plasma Pharmacokinetics and Pharmacodynamics of a New Prodrug N-I-Leucyl doxorubicin and Its Metabolites in a Phase I Clinical Trial, Journal of Clinical Oncology, vol. 10, no. 12, 1897-1906, 1992 | | | |
| <i>JRL</i> | | DE GROOT et al, Synthesis and Biological Evaluation of Novel Prodrugs of Anthracyclines for Selective Activation by the Tumor-Associated Protease Plasmin, J. Med. Chem., 42, 5277-5283, 1999 | | | |
| SAFAVY et al, Paclitaxel Derivatives for Targeted Therapy of Cancer: Toward the Development of Smart Taxanes, J. Med. Chem., 42, 4919-4924, 1999 | | | | | |
| <i>JRL</i> | | NAGASE et al, Human Matrix Metalloproteinase Specificity Studies Using Collagen Sequence-Based Synthetic Peptides, Biopolymers, vol. 40, 399-416, 1996 | | | |
| <i>JRL</i> | | WHITTAKER et al, Design and Therapeutic Application of Matrix Metalloproteinase Inhibitors, Chem. Rev. 99, 2735-2776, 1999 | | | |
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| Examiner Signature | <i>Jeffrey E. Russell</i> | | Date Considered | December 3, 2002 | |

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